REMARKS

Claims 1-34 are pending in the application. Claims 8-10 and 16-33 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention. Claims 1-7 and 11-15 have been rejected.

Claims 1-34 have been cancelled and new claim 35 has been added. Support for the new claim 35 can be found throughout the specification and the claims as originally filed. Specifically, support can be found on page 2, lines 18-19 and the replacement paragraph on page 73, lines 14-15. No new matter has been added by the proposed amendments. Cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to more particularly point out and distinctly claim the invention to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Objections

1. The Examiner objects to claims 1-7, 11-15, and34 for the use of designation "SMARC." This objection is moot in light of the cancellation of claims 1-7, 11-15, and 34. Nonetheless, Applicants point out that new claim 35 has been amended to recite that SMARCD3 comprises SEQ ID No. 5.

2. The Examiner objects to claims 1-7, 11-15, and 34 for use of the language "significant." This objection is moot in light of the cancellation of claims 1-7, 11-15, and34.

3. The Examiner objects to claims 11 and 15 for the use of the language "corresponding to said marker." This objection is moot in light of the cancellation of claims 11 and 15.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph.

Claims 15 is rejected under 35 U.S.C. § 112, second paragraph because it is drawn to "stringent conditions" which is not defined by the claim. This rejection is moot in light of the cancellation of claim 15.

Claim Rejections Under 35 U.S.C. § 101

Claims 1-7, 11-15, and 34 are rejected under 35 U.S.C. § 101 because the Examiner states that the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility. Applicants disagree with the basis of this rejection and respectfully request reconsideration in light of the following remarks.

A. The Examiner states that in "the absence of objective data to support the claimed detecting a difference in the mRNA level of SMARCD-3 in prostate cancer tissue as compared to normal prostate tissue, one cannot assess the claimed method, in view that change in the level of gene expression of a specific gene associated with cancer is an unpredictable event." In addition, the Examiner states that "since change in level of expression of a gene in a tumor as compared to normal corresponding cells is unpredictable, one cannot determine that SMARCD3 would be differentially expressed in prostate cancer tissues versus corresponding normal cells..."

The present invention does have specific, substantial and well-established utility since the experiments described in the specification were performed in a well-recognized *in vitro* model of human prostate cancer which is recognized by those skilled in the art to correlate with *in vivo* human results. The LNCaP cell line, which was established from a metastatic lesion of human prostatic adenocarcinoma, has been widely used in the study of prostate cancer for over 20 years. The enclosed seminal journal article establishes the LNCaP cell line maintains malignant properties, hormonal responsiveness and drug sensitivity of the prostate adenocarcinoma (Horoszewicz, J.S. "LNCaP Model of Human Prostatic Carcinoma" *Cancer Research*, 43, 1809-1818 (1983)). Those skilled in the art view LNCaP cells as an established *in vitro* model of prostate cancer as evidenced by the fact that this seminal article establishing the LNCaP cell line has been cited over 800 times in other peer-reviewed journals (See enclosed Web of Science Cited References Record).

According to MPEP 2164.02, "if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating." (See also, *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995), reversing the PTO decision based on finding that *in vitro* data did not support *in vivo* applications).

In addition, Applicants submit a Declaration of Dr. Steven Haney pursuant to 37 C.F.R. §1.132 as further proof that the claimed methods have utility and were fully enabled by the Specification as filed. This Declaration establishes that one skilled in the art would recognize that the LNCaP cell line model used in the experiments described in the application is a well-characterized model of human prostate cancer. Therefore, one can predict that since SMARCD-3 expression was decreased in the LNCaP cell line model, expression would also be decreased in cancer tissue. Well-characterized human cancer cell lines, such as LNCaP, are routinely used and have proven to be highly predictive of *in vivo* results.

Furthermore, the Declaration states that the Applicants' specification is disclosed in such a manner that one skilled in the art will be able to practice it without undue experimentation. The LNCaP well-established cell line model of human prostate cancer was used to show that SMARCD-3 decreases in expression in prostate cancer cells after androgen treatment. One skilled in the art would appreciate the accuracy with which the cell line model of prostate cancer mimics the genetics of human prostate cancer and further recognize the application's analytical techniques (e.g., RNA extraction, quantitative RT-PCR, western blot analysis, statistical analysis, and tissue microarray analysis) to be well established. One skilled in the art would conclude that the *in vitro* data presented by the applicant is well correlated with the invention as claimed, namely the methods of the invention to diagnose or monitor development or progression of prostate cancer in humans.

B. The Examiner states that the "claimed method, as disclosed in the specification, is based on a flawed method, i.e., using Affymetrix for screening an underepresentative [sic] number of genes...[since]...the cRNAs from a total of 6000 genes of the claimed invention would not be representative of all mRNAs present in a cell."

Applicants submit the Declaration of Dr. Steven Haney pursuant to 37 C.F.R. §1.132 as further proof that one skilled in the art would recognize that genes, which were found to be statistically significantly expressed ($p < 0.05$, using a two-way analysis of variance (ANOVA)) in response to a natural androgen DHT in LNCaP cells based on the Affymetrix Genechip™ screening of 6800 full-length genes, provide specific and substantial utility as a marker for prostate cancer.

The Declaration and above remarks obviate the rejections under 35 U.S.C. § 101. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

A. The Examiner rejects claims 1-7, 11-15 and 34 under 35 U.S.C. § 112, first paragraph for the same reasons they were rejected under 35 U.S.C. § 101.

In response, Applicants respectfully traverse the Examiner's rejection. However, without conceding the Examiner's position, and in order to expedite prosecution, Applicants have canceled claims 1-7, 11-15 and 34 rendering this rejection moot.

The Declaration and above remarks obviate the rejections under 35 U.S.C. § 101 as they apply to new claim 35. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

B. The Examiner states that claims 1-7, 11-15 and 34 are rejected under 35 U.S.C. § 112, first paragraph, for lack of disclosure of the actual sequence structure of SMARCD3.

Although these rejections are moot in light of the cancellation of claims 1-7, 11-15 and 34, Applicants respectfully traverse this rejection to the extent that it may be applicable to the newly presented claim 35.

Applicants point out that new claim 35 specifically recites "SMARCD3 comprises SEQ ID No. 5." Applicants assert that claim 35 is of appropriate scope and is patentable as the structural information for SMARCD3 is quite clearly provided by the sequence of SEQ ID No. 5 itself. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

C. The Examiner rejects claims 1-5, 11-15, and 34 under 35 U.S.C. § 112, first paragraph for lack of enablement for a method for detecting prostate cancer, comprising detected a *difference* in the mRNA level of SMARCD3. While this rejection is moot in light of the cancellation of claims 1-5, 11-15, and 34, Applicants point out that new claim 35 recites "detecting a *decrease* in expression of SMARCD3."

D. The Examiner rejects claims 1, 2, 3, 6, 7, 11-15, and 34 under 35 U.S.C. § 112, first paragraph for lack of enablement of the phrase "any sample." Applicants respectfully traverse the Examiner's rejection. However, without conceding the Examiner's position, and in order to expedite prosecution, Applicants have cancelled the rejected claims. Applicants point out that new claim 35 recites "in a sample of prostate cells." Accordingly, Examiner is respectfully requested to withdraw this rejection.

E. The Examiner rejects claims 11-15 under 35 U.S.C. § 112, first paragraph for lack of enablement of the phrase "a transcribed polynucleotide or portion thereof corresponding to said marker." Applicants respectfully traverse the Examiner's rejection. However, without conceding the Examiner's position, and in order to expedite prosecution, Applicants have cancelled the rejected claims rendering this rejection moot.

CONCLUSION

In summary, the above-identified patent application has been amended and reconsideration is respectfully requested for all the reasons set forth above. In the event that the amendments and remarks are not deemed to overcome the grounds for rejection, the Examiner is kindly requested to telephone the undersigned representative to discuss any remaining issues.

Respectfully submitted,

NUTTER McCLENNEN & FISH, LLP

Date: December 10, 2004

Thomas J. Engellenner
Registration No.: 28,711
Attorney for Applicants
World Trade Center West
155 Seaport Boulevard
Boston, MA 02210-2604
Tel: (617) 439-2948
Fax: (617) 310-9948

1379237.1